

CLAIMS

1. A method of diagnosing or prognosticating a neurodegenerative disease in a subject, or determining whether a subject is at increased risk of developing said disease, comprising determining a level and/or an activity of

- (i) a transcription product of the StAR gene, and/or
- (ii) a translation product of the StAR gene, and/or
- (iii) a fragment, or derivative, or variant of said transcription or translation product,

in a sample from said subject and comparing said level and/or said activity to a reference value representing a known disease or health status, thereby diagnosing or prognosticating said neurodegenerative disease in said subject, or determining whether said subject is at increased risk of developing said neurodegenerative disease.

2. The method according to claim 1 wherein said neurodegenerative disease is Alzheimer's disease.

3. A kit for diagnosing or prognosticating a neurodegenerative disease, in particular Alzheimer's disease, in a subject, or determining the propensity or predisposition of a subject to develop such a disease, said kit comprising:

- (a) at least one reagent which is selected from the group consisting of (i) reagents that selectively detect a transcription product of the StAR gene and (ii) reagents that selectively detect a translation product of the StAR gene and
- (b) an instruction for diagnosing or prognosticating a neurodegenerative disease, in particular Alzheimer's disease, or determining the propensity or predisposition of a subject to develop such a disease by (i) detecting a level, or an activity, or both said level and said activity, of said transcription product and/or said translation product of the StAR gene, in a sample from said subject; and (ii) diagnosing or prognosticating a neurodegenerative disease, in particular Alzheimer's disease, or determining the propensity or predisposition of said subject to develop such a disease, wherein a varied level, or activity, or both said level and said activity, of said transcription product and/or said translation product compared to a reference value representing a known health status; or a level, or activity, or both said level and said activity, of said transcription product and/or said translation product similar or equal to a reference value

representing a known disease status indicates a diagnosis or prognosis of a neurodegenerative disease, in particular Alzheimer's disease, or an increased propensity or predisposition of developing such a disease.

4. A modulator of an activity and/or of a level of at least one substance which is selected from the group consisting of

- (i) the StAR gene, and/or
- (ii) a transcription product of the StAR gene, and/or
- (iii) a translation product of the StAR gene, and/or
- (iv) a fragment, or derivative, or variant of (i) to (iii).

5. A recombinant, non-human animal comprising a non-native gene sequence coding for StAR, or a fragment, or a derivative, or a variant thereof, said animal being obtainable by:

- (i) providing a gene targeting construct comprising said gene sequence and a selectable marker sequence, and
- (ii) introducing said targeting construct into a stem cell of a non-human animal, and
- (iii) introducing said non-human animal stem cell into a non-human embryo, and
- (iv) transplanting said embryo into a pseudopregnant non-human animal, and
- (v) allowing said embryo to develop to term, and
- (vi) identifying a genetically altered non-human animal whose genome comprises a modification of said gene sequence in both alleles, and
- (vii) breeding the genetically altered non-human animal of step (vi) to obtain a genetically altered non-human animal whose genome comprises a modification of said endogenous gene, wherein said disruption results in said non-human animal exhibiting a predisposition to developing symptoms of a neurodegenerative disease or related diseases or disorders.

6. An assay for screening for a modulator of neurodegenerative diseases, in particular Alzheimer's disease, or related diseases or disorders of one or more substances selected from the group consisting of

- (i) the StAR gene, and/or
- (ii) a transcription product of the StAR gene, and/or
- (iii) a translation product of the StAR gene, and/or
- (iv) a fragment, or derivative, or variant of (i) to (iii),

said method comprising:

- (a) contacting a cell with a test compound;
- (b) measuring the activity and/or level of one or more substances recited in (i) to (iv);
- (c) measuring the activity and/or level of one or more substances recited in (i) to (iv) in a control cell not contacted with said test compound; and
- (d) comparing the levels and/or activities of the substance in the cells of step (b) and (c), wherein an alteration in the activity and/or level of substances in the contacted cells indicates that the test compound is a modulator of said diseases or disorders.

7. A method of screening for a modulator of neurodegenerative diseases, in particular Alzheimer's disease, or related diseases or disorders of one or more substances selected from the group consisting of

- (i) the StAR gene, and/or
- (ii) a transcription product of the StAR gene, and/or
- (iii) a translation product of the StAR gene, and/or
- (v) a fragment, or derivative, or variant of (i) to (iii),

said method comprising:

- (a) administering a test compound to a test animal which is predisposed to developing or has already developed symptoms of a neurodegenerative disease or related diseases or disorders in respect of the substances recited in (i) to (iv);
- (b) measuring the activity and/or level of one or more substances recited in (i) to (iv);
- (c) measuring the activity and/or level of one or more substances recited in (i) or (iv) in a matched control animal which is predisposed to developing or has already developed a neurodegenerative disease or related diseases or disorders in respect to the substances recited in (i) to (iv) and to which animal no such test compound has been administered;
- (d) comparing the activity and/or level of the substance in the animals of step (b) and (c), wherein an alteration in the activity and/or level of substances in the test animal indicates that the test compound is a modulator of said diseases or disorders.

8. The method according to claim 7 wherein said test animal and/or said control animal is a recombinant animal which expresses StAR, or a fragment, or a derivative, or a variant thereof, under the control of a transcriptional control element which is not the native StAR gene transcriptional control element.

9. An assay for testing a compound, preferably for screening a plurality of compounds for inhibition of binding between a ligand and a translation product of the StAR gene, or a fragment, or a derivative, or a variant thereof, said assay comprising the steps of:

- (i) adding a liquid suspension of said translation product of the StAR gene, or a fragment, or derivative, or variant thereof, to a plurality of containers;
- (ii) adding a compound or a plurality of compounds to be screened for said inhibition to said plurality of containers;
- (iii) adding a detectable, preferably a fluorescently labelled ligand to said containers;
- (iv) incubating said translation product of the StAR gene, or said fragment, or derivative, or variant thereof, and said compound or compounds, and said detectable, preferably fluorescently labelled ligand;
- (v) measuring amounts of preferably fluorescence associated with said translation product of the StAR gene, or with said fragment, or derivative, or variant thereof; and
- (vi) determining the degree of inhibition by one or more of said compounds of binding of said ligand to said translation product of the StAR gene, or said fragment, or derivative, or variant thereof.

10. A protein molecule, said protein molecule being a translation product of the StAR gene, SEQ ID NO. 1, or a fragment, or derivative, or variant thereof, for use as a diagnostic target for detecting a neurodegenerative disease, preferably Alzheimer's disease.

11. A protein molecule, said protein molecule being a translation product of the StAR gene, SEQ ID NO. 1, or a fragment, or derivative, or variant thereof, for use as a screening target for reagents or compounds preventing, or treating, or ameliorating a neurodegenerative disease, preferably Alzheimer's disease.

12. Use of an antibody specifically immunoreactive with an immunogen, wherein said immunogen is a translation product of the StAR gene, SEQ ID NO. 1, or a fragment, or derivative, or variant thereof, for detecting a pathological state of a cell in a sample from a subject, comprising immunocytochemical staining of said cell with said antibody, wherein an altered degree of staining, or an altered staining pattern in said cell compared to a cell representing a known health status indicates a pathological state of said cell.